Toxoplasma IgG Expressed in a Patient With Rosai-Dorfman Disease

Hung-Ju Liao and Ching-Wen Chiang
Department of Otolaryngology, Lo Tung Poh-Ai Hospital, Ilan, Taiwan.

Rosai-Dorfman Disease (RDD) is a rare benign disease characterized by sinus histiocytosis with massive lymphadenopathy. RDD can be differentiated from other types of histiocytosis by immunochemical analysis, as RDD is positive for S100. Conversely, toxoplasmosis lymphadenitis is characterized by clusters of epithelioid histiocytes in lymphoid tissue, with mixed lymphocytic and immunoblastic cell populations. The serology data could help in diagnosing toxoplasmosis lymphadenitis, as the toxoplasma IgG should be positive. Here we present the rare case of a 73-year-old woman who presented with a left parotid mass and multiple neck lymphadenopathy that initially had been diagnosed as toxoplasmosis lymphadenitis from a positive result on serology examination, but was finally proven to be RDD based on immunochemical results. We also discuss the relationship between RDD and toxoplasmosis in this case.

Key Words: parotid tumor, Rosai-Dorfman disease, toxoplasmosis lymphadenopathy
(*Kaohsiung J Med Sci* 2010;26:373–6)

Neck lymphadenopathy with histiocytosis can result in many differential diagnoses, such as Rosai-Dorfman disease (RDD), toxoplasmosis lymphadenitis, Wegener granulomatosis and other various histiocytoses. Although the definite diagnosis depends on histopathological examination, a thorough examination of the disease depending on clinical presentation is still essential. To make a definite diagnosis, S100 immunochemical staining must be performed in cases of suspected RDD [1], and toxoplasma IgG must be checked in cases of suspected toxoplasmosis lymphadenitis [2]. Both would require a clinical suspicion of the diseases as S100 and toxoplasma IgG determination are not routinely performed in practice. Here we present a case with diffuse neck lymphadenopathies and a left parotid mass that had initially been diagnosed as toxoplasmosis lymphadenitis, but later was diagnosed as RDD.

Case Presentation

A 73-year-old woman, who denied any systemic disease, noted a mass of about 1 cm in her left upper neck for several months. The mass was painful and slow-growing. She came to our outpatient department and a left parotid mass was suspected. The computed tomography scan with contrast revealed an intraparotid lymph node (Figure 1) with bilateral multiple cervical lymph nodes. An excisional biopsy of the left intraparotid node was made and the histopathology examination revealed chronic lymphadenitis (Figure 2), with enlarged, hyperplastic lymphoid follicles and prominent germinal centers. Histiocyte infiltration was also seen in the sinusoids, fibrous stroma and fibrous capsule.

The postoperative course was smooth and the patient was regularly followed up at the outpatient department. However, the tenderness in the left parotid

Received: Sep 16, 2009 Accepted: Dec 28, 2009
Address correspondence and reprint requests to: Dr Ching-Wen Chiang, 83 Nan Chang Street, Lotung, Yilan 265, Taiwan.
E-mail: acuteshin@pchome.com.tw

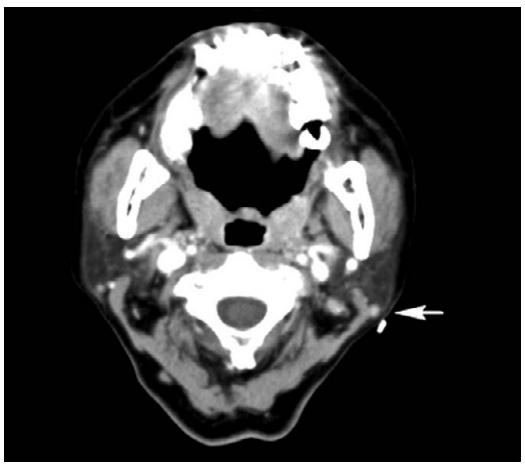

Figure 1. *Computed tomography scan with contrast revealed an intraparotid lymph node (arrow).*

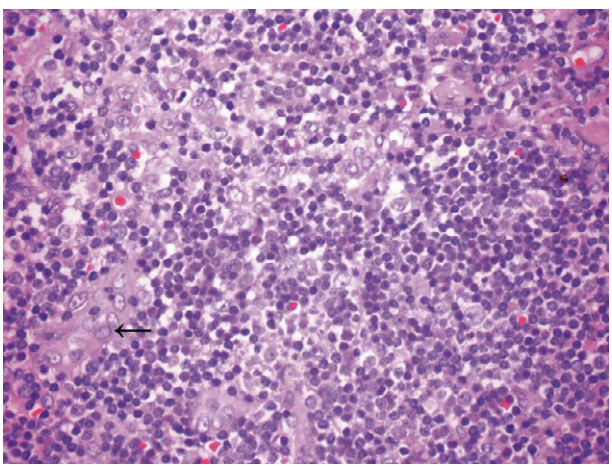

Figure 2. *Histopathology examination revealed chronic lymphadenitis and histiocyte infiltration in the sinusoids (arrow).*

area recurred about half a year after the surgery. We check the toxoplasma IgG level for an endemic cause, although the patient denied any animal exposure and travelling history. The serologic result was positive (28.3 IU/mL). The patient then received sulfamethoxazole/trimethoprim for treatment of toxoplasmosis.

The left parotid tenderness persisted despite antibiotic treatment. The computed tomography scan continued to show a left intraparotid node with multiple neck lymphadenopathy. The patient received an excisional biopsy of the left intraparotid node again and the histopathology also revealed a picture of chronic lymphadenitis. This time, the S100 stain was performed and revealed a positive result (Figure 3).

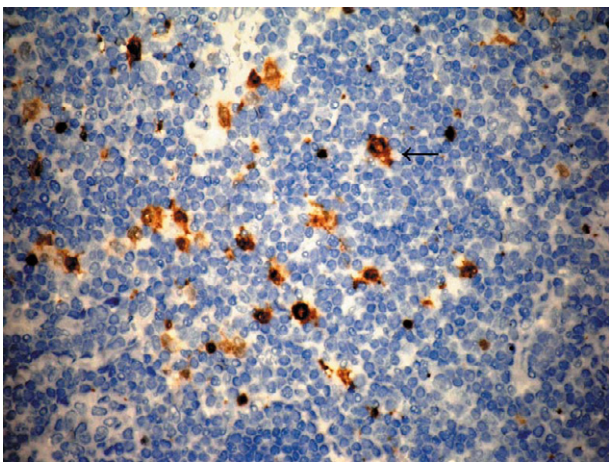

Figure 3. *Immunostaining revealed positive S100 protein of the lymph lymphoid tissue (arrow).*

The previous specimen was reviewed and stained for S100. The result was also positive. Hence RDD was diagnosed. The patient then received oral steroid therapy at the outpatient department. No recurrence of the neck mass was noted during follow up.

Discussion

RDD is a rare, benign, idiopathic and non-neoplastic histiocytic disorder, which is characterized by the overproduction of histiocytes and accumulation in lymph nodes throughout the body. It was first recognized as a distinct clinicopathologic entity by Rosai and Dorfman in 1969 [3]. The clinical features of RDD include painless lymphadenopathy, mostly involving the cervical region, and sometimes with extranodal involvement such as skin, nasal cavity and paranasal sinuses, eye and orbit, bones and many other less frequently reported sites. The histopathological feature of RDD includes expanded sinuses of the lymph nodes with predominance of histiocytes, which have prominent vesicular nuclei, and cytoplasm filled with lymphocytes. The most useful immunohistologic marker for RDD is the expression of the S100 protein on histiocytes [1]. S100 is a characteristic marker for dendritic cells in lymph nodes and Langerhans cells in skin. A combination of the clinical features and the S100 stain on histopathological examination aids in diagnosis of RDD. In our case, the histopathological feature of RDD was not typical, but the positive S100 stain led to the diagnosis of RDD.

Conversely, toxoplasmosis, which is caused by the parasite of *Toxoplasma gondii*, is an infectious disorder acquired by ingestion of cysts in infected meat or oocysts that may contaminate food, water and soil. Most acute acquired infection cases do not experience obvious symptoms or signs, although some may experience malaise, low-grade fever, and cervical lymphadenopathy [4]. The histopathological features of toxoplasmosis lymphadenitis are follicular hyperplasia and microgranulomas which contain less than 25 epithelioid cell nuclei [5]. The parasite itself was seldom found in the specimen. The diagnosis is often confirmed by the patient's serology test. Although toxoplasma IgM has to be the marker of acute infection, it has high false positive rates in non-reference level laboratories, thus resulting in its uselessness in clinical practice [2]. In contrast to IgM, toxoplasma IgG is more reliable and can help in making the diagnosis of toxoplasmosis. In our patient, the toxoplasma IgG test was positive and this led us to the initial diagnosis of toxoplasmosis lymphadenitis.

The etiology of RDD remains uncertain. Proposed mechanisms included an occult chronic infection, or an exaggerated immune response to infection, or an antigen that causes a proliferation of histiocytes [1]. *In situ* DNA hybridization has demonstrated herpesvirus-6-specific DNA within histiocytes of the RDD [6], but the relationship of herpesvirus-6 and RDD remains uncertain. In our case, it is possible that chronic infection with *T. gondii* could lead to an overproduction of histiocytes, and finally to presentation of RDD. Of course, more cases and studies are necessary to confirm our hypothesis.

The treatment courses of RDD and toxoplasmosis lymphadenitis are very different and even present a mutual conflict. Most patients with RDD have a complete and spontaneous remission, and some may experience recurrent or persistent but stable lymphadenopathy. If treatment is given, a combination of corticosteroids and immunosuppressants are often used [7]. As with toxoplasmosis lymphadenitis, treatment is usually not needed if it turns out to be asymptomatic. If treatment is given, the combination of sulfadiazine, pyrimethamine and folinic acid are often recommended. Other antibiotics such as clindamycin and spiramycin could also be used [4]. In our practical experience, we often use sulfamethoxazole/trimethoprim. In our case, it was important to make the definite diagnosis of RDD, because the use of steroids is in conflict with the treatment of toxoplasmosis lymphadenitis.

In conclusion, for patients with cervical or intraparotid lymphadenopathies, the S-100 stain on histopathology and toxoplasma IgG on serology should both be examined to differentiate between toxoplasmosis lymphadenitis and RDD.

References

1. Gaitonde S. Multifocal, extranodal sinus histiocytosis with massive lymphadenopathy: an overview. *Arch Pathol Lab Med* 2007;131:1117–21.
2. Montoya JG. Laboratory diagnosis of Toxoplasma gondii infection and toxoplasmosis. *J Infect Dis* 2002; 185(Suppl 1):S73–82.
3. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy: a newly recognized benign clinical entity. *Arch Pathol* 1969;87:63–70.
4. Montoya JG, Remington JS. Management of *Toxoplasma gondii* infection during pregnancy. *Clin Infect Dis* 2008; 47:554–66.
5. Eapen M, Mathew CF, Aravindan KP. Evidence based criteria for the histopathological diagnosis of toxoplasmic lymphadenopathy. *J Clin Pathol* 2005;58:1143–6.
6. Luppi M, Barozzi P, Garber R, et al. Expression of human herpesvirus-6 antigens in benign and malignant lymphoproliferative diseases. *Am J Pathol* 1998;153: 815–23.
7. Fu CH, Huang SF, Jung SM, et al. Radiology quiz case 2. Extranodal Rosai-Dorfman disease involving the right orbit and nasal cavity. *Arch Otolaryngol Head Neck Surg* 2009;135:317,319.

弓漿蟲感染之 IgG 陽性表現於 Rosai-Dorfman 氏病

廖宏儒 蔣敬文

羅東博愛醫院 耳鼻喉科

Rosai-Dorfman 氏病為一罕見良性疾病，其病理特徵為廣泛性淋巴結內有組織球浸潤，在免疫染色上呈現 **S100** 陽性，而弓漿蟲感染所造成之淋巴結病變其病理表現則為類上皮組織球群聚，而血清檢查則會呈現弓漿蟲 **IgG** 抗體陽性，在此我們報告一例 **73** 歲女性，初始表現為左側腮腺腫瘤伴隨兩側頸部淋巴結病變，經血清學檢查初診斷為弓漿蟲感染所造成之淋巴結病變，但最後經免疫染色確定為 **Rosai-Dorfman** 氏病，我們假設弓漿蟲感染和 **Rosai-Dorfman** 氏病可能存在相關性。

關鍵詞：腮腺腫瘤，**Rosai-Dorfman** 氏病，弓漿蟲淋巴結病變

（高雄醫誌 **2010;26:373–6**）

收文日期：**98** 年 **9** 月 **16** 日

接受刊載：**98** 年 **12** 月 **28** 日

通訊作者：蔣敬文醫師

羅東博愛醫院耳鼻喉科

265 宜蘭縣羅東鎮南昌街 **83** 號